should be preceded by an ECG to exclude those patients with atrioventricular block grades II and III.

[1] Singh, B N, and Hauswirth, O, *American Heart Journal*, 1974, **87,** 367.
[2] Beermann, B, Edhag, O, and Vallin, H, *British Heart Journal*, 1975, **37,** 668.
[3] Lagergren, H, and Johansson, L, *Acta Chirurgica Scandinavica*, 1963, **125,** 562.
[4] Michaeli, E, and Rosén, A, *Acta Medica Scandinavica*, 1968, **183,** 401.
[5] Steiner, C, *et al*, *Journal of Pharmacology and Experimental Therapeutics*, 1970, **173,** 323.
[6] Rawlins, M D, *et al*, *European Journal of Clinical Pharmacology*, 1975, **8,** 91.
[7] Corday, E, *et al*, *Geriatrics*, 1971, **26,** 78.

(*Accepted 27 April 1978*)

Sulphamethoxazole, hypoalbuminaemia, crystalluria, and renal failure

Sulphamethoxazole is an active component of co-trimoxazole. We describe two patients who developed renal failure after receiving this drug.

Case reports

Case 1—A 31-year-old woman developed generalised peritonitis secondary to a pyosalpinx, which had been excised. Endotoxic shock ensued, which was treated with penicillin, gentamicin, and metronidazole for seven days with good effect. She then became febrile and was started on co-trimoxazole intravenously, 1 ampoule (5 ml co-trimoxazole in 150 ml 0·9% saline) infused over 30 minutes. The drug was given 12-hourly, and within 36 hours her urine output had fallen in association with haematuria and profound crystalluria. Co-trimoxazole was stopped but she went into complete renal failure and, despite acute haemodialysis, died.

Case 2—A 24-year-old man presented with peritonitis eight days after being stabbed in the abdomen causing three colonic perforations, which had been oversewn. He was given the same antibiotics as in case 1, but with little effect, and intravenous co-trimoxazole was begun (same regimen as in case 1). Within 48 hours he went into acute renal failure. Mannitol (20%) 300 ml was administered and co-trimoxazole stopped. This resulted in a pronounced diuresis, and within 14 days renal function returned to normal.

Comment

Both these patients were septicaemic and hypoproteinaemic (serum albumin concentrations 16 and 18 g/l respectively). In both cases serum samples taken before co-trimoxazole treatment were recovered, which permitted in-vitro sulphamethoxazole-binding studies using ^{35}C-sulphamethoxazole. With normoalbuminaemic serum 24-35% of sulphamethoxazole is protein bound.[1] In these two patients, however, only 2% and 3·6% of the drug was bound. Neither patient was dehydrated when co-trimoxazole was instituted, and in both cases renal function was normal (serum creatinine 97·2 and 79·6 μmol/l (1·1 and 0·9 mg/100 ml) respectively). Presumably by virtue of the hypoalbuminaemia, and possibly due to the presence of penicillin and metronidazole in the serum acting as competitive binders, sulphamethoxazole was unable to bind, so that nearly all the drug was free (unbound). This is a similar finding to that reported in kwashiorkor serum, in which only 4·7% of the drug was bound (serum albumin 22 g/l).[1]

As only the free component of a drug is filtered by the kidneys it may be assumed that in these two patients crystalluria ensued secondary to the massive load of free drug. Hence co-trimoxazole should probably be used with circumspection in hypoalbuminaemic patients. If it is essential to use the drug, the dosage should be decreased, the dosage frequency increased, and great care paid to fluid therapy.

[1] Buchanan, N, *South African Medical Journal*, 1977, **52,** 733.

(*Accepted 26 April 1978*)

Intensive Care Unit, Baragwanath Hospital, Johannesburg
N BUCHANAN, FCP(SA), consultant paediatrician

SHORT REPORTS

Stimulated sweating in chronic renal failure

Concentrations of urea and potassium in the sweat of normal subjects and patients with chronic renal failure (CRF) are higher than serum concentrations.[1-3] Water loss from the skin may exceed two litres per hour in hot environments.[2 4 5] It would therefore be interesting to examine the extent to which stimulated sweating in patients with CRF could compensate for loss of renal function. We describe a patient on chronic intermittent haemodialysis who was used to taking sauna baths. Serum concentrations of urea and potassium were low and weight gain between haemodialysis sessions was small compared with those of other patients undergoing intermittent haemodialysis. Losses of urea, potassium, and water in sauna and hot baths[5] were measured to investigate whether they could account for the observed low serum concentrations of these substances and for the stable fluid balance in this patient.

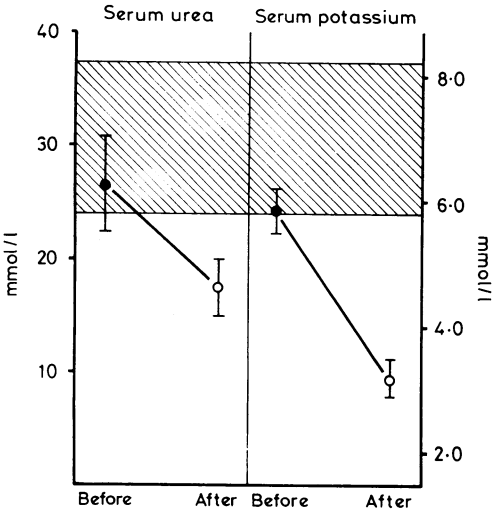
Patient, methods, and results

A 52-year-old anuric man started to take sauna baths three times a week on days when he was not undergoing dialysis six months before our study. Before the sauna baths the patient took a lukewarm shower and brushed his skin to remove formerly excreted solids. The air temperature in the sauna was 70°C, and he bathed for one to two hours. After each sauna bath his body weight decreased by 1·5-2 kg. During the study the sweat that dripped from his bended head while in the sauna was collected in 20-ml samples, and total losses of urea and potassium were calculated from weight loss and sweat concentrations. The patient was also studied in hot water baths of 42°C.[5] He was immersed in water up to his neck in an impermeable plastic bag, which contained 20 litres of distilled water. Fluid from the bag was sampled before and after the baths and duplicate 1-litre portions were concentrated tenfold by distillation. This permitted us to calculate more accurately the total loss of urea and potassium than in the sauna bath.

The figure shows predialysis serum concentrations of urea and potassium in the patient and in 16 controls on chronic intermittent haemodialysis. Results were corrected for differences in dietary intake related to body weight. After six months serum urea and potassium concentrations were significantly lower in the patient than in the controls ($P < 0·001$; t-test). The sweat to serum urea ratio was 2·0 in two sauna baths and 1·8 in two hot water baths. Sweat to serum potassium ratio was 2·5 for both sauna and hot water baths. Sweat rates in sauna and hot water baths were 21 and 33 ml/min respectively. Urea clearances in hot water baths were therefore higher than in sauna baths—56 and 40 ml/min respectively. Calculated losses of urea and potassium in sweat were 43 and 12 mmol/h (2·6 g/h and 12 mEq/h) compared with 117 and 20 mmol/h (7·0 g/h and 20 mEq/h) by haemodialysis. Total excretion of urea and potassium in sweat averaged 215 and 60 mmol/week (12·9 g/week and 60 mEq/week) respectively, which amounted to 19% and 30% of the total quantity removed by haemodialysis. These figures fully explain the observed falls in serum concentrations of urea and potassium of 23% and 35% respectively.

Comment

These findings indicate that stimulated sweating can be used as a valuable adjunct to chronic intermittent haemodialysis. In our patient a 30-minute hot water bath every day was as effective as a two-hour sauna bath three times a week. In patients with CRF control of fluid



Serum urea and potassium concentrations in patient with CRF before (●) and six months after (○) period when he took sauna baths three times a week. His diet contained 55 g protein, 50 mmol potassium, and 800 ml fluid before and 60 g protein, 90 mmol potassium, and a free fluid intake after six months. Mean results (±SD) (n=14) are compared with values in 16 control subjects (n=140; shaded area). Patients who needed polysterene sulphonate to control serum potassium were not included. All values were measured before dialysis and were converted to 70 kg of body weight, 100 g daily protein intake, and 70 mmol potassium intake.

Conversion: SI to traditional units—Urea: 1 mmol/l ≈ 6 mg/100 ml. Potassium: 1 mmol/l = 1 mEq/l.

balance, uraemia, and hyperkalaemia can be facilitated by this mode of treatment, which might obviate the need for strict dietary regulations and thereby improve quality of life in these patients.

We thank Professor J de Graeff and Dr M A D H Schalekamp for their advice and criticism.

[1] Dittmer, D S, (editor), *Blood and Other Body Fluids*. Federation of the American Society for Experimental Biology, 1961.
[2] Schwarts, I L, in *Mineral Metabolism*, ed C L Comar and F Bromer, part I, section A, p 346. New York, Academic Press, 1960.
[3] Snyder, D, and Merrill, J P, *Transactions of the American Society for Artificial Internal Organs*, 1966, **12**, 188.
[4] Kuno, Y, *Human Perspiration*. Springfield, Illinois, Thomas, 1956.
[5] Fujishima, K, and Kosake, M, *Nagoya Medical Journal*, 1971, **17-I**, 25.

(*Accepted 30 March 1978*)

Department of Internal Medicine I, University Hospital, Erasmus University, Rotterdam
A J MAN IN 'T VELD, MD, medical registrar

Department of Internal Medicine, Division of Nephrology, University Hospital, Leiden
J H VAN MAANEN, MD, PHD, medical registrar
I M SCHICHT, MD, consultant physician

Inosine in preserving renal function during ischaemic renal surgery

The purine nucleoside inosine provides excellent protection for the kidney during warm ischaemia in rats[1] and dogs.[2] Renal function after warm ischaemia was significantly better than in controls, and rapid post-ischaemic resynthesis of tissue adenosine triphosphate (ATP) occurred in inosine-protected kidneys,[1] providing further evidence of the maintenance of renal cellular function.

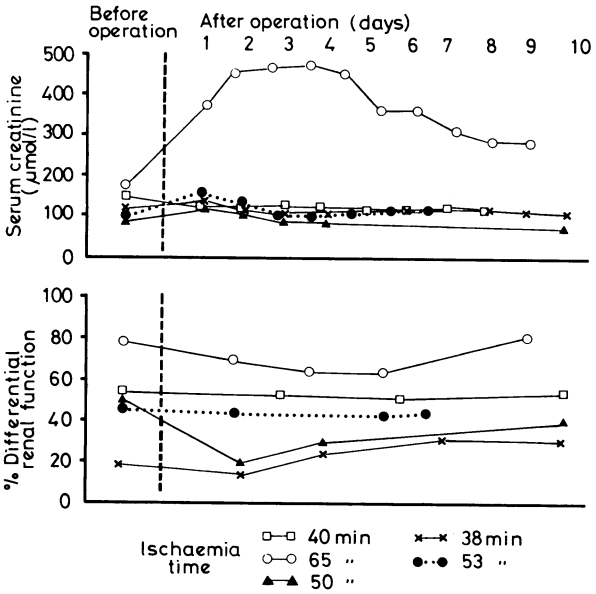
Intravenous pretreatment with inosine in rats protected the kidney for up to 120 minutes of warm ischaemia.[3] Dog kidneys protected by inosine excreted significantly less γ-glutamyltranspeptidase in the urine than untreated controls after 90 minutes of warm ischaemia. This enzyme is present in high concentration in the renal tubular brush border and is released with cellular disruption. Electron microscopy studies of inosine-protected kidneys showed good preservation of this area of the nephron (unpublished observations).

This experimental evidence encouraged us to use inosine clinically. For the animal work we used a laboratory grade of inosine (Sigma, London). For clinical purposes we used a pharmaceutically available preparation of inosine[4] (Trophicardyl, Laboratoire Chantereau, 94114 Arcueil, France) which we had shown in evaluation in animals to be as effective as inosine.

Methods

Conservative renal surgery under ischaemic conditions was performed in four patients with staghorn calculi and in a fifth for bilateral renal tumours. The kidney was exposed and the renal artery isolated and occluded with a bull-dog clamp. A fine cannula was inserted into the renal artery distal to the clamp and the kidney perfused with 80 ml of a 2·5% solution of inosine (Trophicardyl) at room temperature; the renal vein was then occluded with a second bull-dog clamp. Blood pressure and pulse rate were monitored throughout. On completion of the procedure the vascular clamps were removed. Overall renal function was assessed before and after operation by serum creatinine measurements; differential renal function was measured by serial gamma camera renography.[5]

The results of serum creatinine measurements before and after operation and the differential renal function estimations are shown in the figure.



Serum creatinine concentrations before and after operation and serial measurements of differential renal function in five patients. *Conversion: SI to traditional units*—Serum creatinine: 1 μmol/l ≈ 0·01 mg/100 ml.

Initial minimal increases in serum creatinine concentration and slight depression of function on renography returned to preoperative values within a few days. Electrolytes remained stable throughout but a transient rise in the serum urate concentration was noted. Reflow of blood on declamping was faster after inosine than after operative protection with hypothermia. No adverse cardiodynamic effects were observed in any patient.

Comment

These results confirm our experimental findings of the protective effect of inosine on the warm ischaemic kidney. The clinical results with inosine are as good as those observed in patients undergoing ischaemic renal surgery with hypothermic protection. The relative simplicity of the inosine technique compared with hypothermic protection has encouraged us to continue with clinical inosine perfusion when a bloodless field is needed for conservative renal surgery for up to 75 minutes.